WHAT IS CLAIMED IS:

1. A recombinant non-human animal in which a *lats* gene has been inactivated by a method comprising introducing a nucleic acid into the animal, or an ancestor thereof, which nucleic acid comprises a non-*lats* sequence flanked by *lats* genomic sequences that promote homologous recombination, such that said non-*lats* sequence replaces the nucleotide sequence encoding the Lats C-terminal domain 1, the Lats C-terminal domain 2, the Lats C-terminal domain 3, and a portion of the kinase domain of the lats protein encoded by the *lats* gene.

2. The recombinant non-human animal of claim 1 in which the non-*lats* sequence replaces the nucleotide sequence encoding the amino acids that correspond to amino acids 756-1130 of human lats, as depicted in Figure 12 (SEQ ID NO:2).

3. The recombinant non-human animal of claim 1 which is a mouse.

4. The recombinant non-human animal of claim 3 in which the *lats* gene contains a lats coding sequence of SEQ ID NO:3.

5. The recombinant non-human animal of claim 1 in which both alleles of the *lats* gene have been inactivated.

6. A method for screening a potential therapeutic compound for activity in treating or preventing cancer comprising administering the compound to the recombinant non-human animal of claim 1; and comparing the size or progression of the cancer in the recombinant non-human animal to which the compound was administered with the size or progression of the cancer in the same recombinant non-human animal prior to administration of the compound or in a recombinant non-human animal that was not so administered or to a standard size or progression of the cancer for such same or a recombinant non-human animal that was not so administered, wherein a decrease in the size or progression of the cancer in the recombinant non-human animal administered the compound as compared to the same animal prior to the administration or to the recombinant non-human animal not so administered or to the standard size or progression of the cancer, indicates that the compound has activity in treating or preventing cancer.

7. The method of claim 6 in which the non-*lats* sequence replaces the nucleotide sequence encoding the amino acids that correspond to amino acids 756-1130 of human lats, as depicted in Figure 12 (SEQ ID NO:2).

8. The method of claim 6 in which the recombinant non-human animal is a mouse.

9. The method of claim 8 in which the *lats* gene contains the lats coding sequence of SEQ ID NO:3.

10. The method of claim 6 in which both alleles of the *lats* gene have been inactivated.

11. The method of claim 6 in which the compound is screened for activity in treating or preventing soft tissue sarcomas.

12. The method of claim 6 in which the compound is screened for activity in treating or preventing ovarian tumors.

13. A method for screening a potential therapeutic compound for activity in treating or preventing cancer comprising recombinantly expressing the compound in the recombinant non-human animal of claim 1; and comparing the size or progression of the cancer in the recombinant non-human animal in which the compound was expressed with the size or progression of the cancer in the same recombinant non-human animal prior to expression of the compound or in a recombinant non-human animal in which the compound was not so expressed or to a standard size or progression of the cancer for such same or a recombinant non-human animal in which the compound was not so expressed, wherein a decrease in the size or progression of the cancer in the recombinant non-human animal in which the compound was expressed as compared to the same animal prior to the expression of the compound or to the recombinant non-human animal in which said compound was not so expressed or to the standard size or progression of the cancer, indicates that the compound has activity in treating or preventing cancer.

14. A method for screening a potential therapeutic compound for activity in treating or preventing skin cancer comprising administering the compound to a *lats* knock-out animal having skin tumors induced by exposure to at least one carcinogen; and comparing the size or progression of the skin tumors on the *lats* knock-out animal to which the compound was administered with the size or progression of skin cancers on the same *lats* knock-out animal prior to administration of the compound or on a *lats* knock-out animal in which skin tumors have also been induced by exposure to said at least one carcinogen but which has not been administered the compound or to a standard size or progression of the skin tumors for such same or a *lats* knock-out animal that was not so administered, wherein a reduction in the size or progression of the skin tumors in the *lats* knock-out animal administered the compound as compared to the same animal prior to

administration of the compound or to the animal not so administered or to the standard size or progression of the skin tumors, indicates that the compound has activity in treating or preventing skin cancer.

15. The method of claim 14 in which the *lats* knock-out animal has at least one *lats* gene which was inactivated by promoting homologous recombination between *lats* genomic sequences and a nucleic acid having non-*lats* sequences flanked by genomic sequences.

16. The method of claim 15 in which the non-*lats* sequence replaces the nucleotide sequence encoding the Lats C-terminal domain 1, the Lats C-terminal domain 2, the Lats C-terminal domain 3, and a portion of the kinase domain of the lats protein encoded by the *lats* gene.

17. The method of claim 15 in which the non-*lats* sequence replaces the nucleotide sequence1 encoding the amino acids that correspond to amino acids 756-1130 of human lats, as depicted in Figure 12 (SEQ ID NO:2).

18. The method of claim 14 in which the *lats* knock-out animal is a mouse.

19. The method of claim 18 in which the *lats* gene contains the lats coding sequence of SEQ ID NO:3.

20. The method of claim 14 in which both alleles of the *lats* gene have been inactivated.

21. The method of claim 14 in which the skin tumors were induced by 9,10-dimethyl-1,2-benzanthracene and repeated exposure to ultraviolet B radiation.

22. The method of claim 14 in which the potential therapeutic compound is administered topically.

23. A method for screening a potential therapeutic compound for activity in treating or preventing skin cancer comprising recombinantly expressing the compound in a *lats* knock-out animal having skin tumors induced by exposure to at least one carcinogen; and comparing the size or progression of the skin tumors on the *lats* knock-out animal in which the compound was expressed with the size or progression of skin cancers on the same *lats* knock-out animal prior to expression of the compound or on a *lats* knock-out animal in which skin tumors have also been induced by exposure to said at least one carcinogen but in which the compound has not been expressed or to a standard size or progression of the skin

tumors for such same or a *lats* knock-out animal in which the compound was not so expressed, wherein a reduction in the size or progression of the skin tumors in the *lats* knock-out animal in which the compound was expressed as compared to the same animal prior to expression of the compound or to the animal in which the compound was not so expressed or to the standard size or progression of the skin tumors, indicates that the compound has activity in treating or preventing skin cancer.

24. A method for screening a potential therapeutic compound for activity in treating or preventing a disease or disorder associated with pituitary dysfunction comprising administering the compound to a *lats* knock-out animal; and comparing the level of an indicator of pituitary dysfunction in the *lats* knock-out animal to which the compound has been administered to the level of the indicator in the same *lats* knock-out animal prior to administration of the compound or to a *lats* knock-out animal that has not been administered the compound or to a standard level of the indicator for such same or a *lats* knock-out animal that was not so administered, wherein a change in the indicator toward the level of the indicator in a wild type animal not afflicted with a pituitary dysfunction as compared to the same animal prior to administration of the compound or to the animal not so administered or to the standard level of the indicator, indicates that the compound is active to treat or prevent a disease or disorder associated with pituitary dysfunction.

25. The method of claim 24 in which the *lats* knock-out animal has at least one *lats* gene which was inactivated by promoting homologous recombination between *lats* genomic sequences and a nucleic acid having non-*lats* sequences flanked by genomic sequences.

26. The method of claim 25 in which the non-lats sequence replaces the nucleotide sequence encoding the Lats C-terminal domain 1, the Lats C-terminal domain 2, the Lats C-terminal domain 3, and a portion of the kinase domain of the lats protein encoded by the *lats* gene.

27. The method of claim 25 in which the non-*lats* sequence replaces the nucleotide sequence encoding the amino acids that correspond to amino acids 756-1130 of human lats, as depicted in Figure 12 (SEQ ID NO:2).

28. The method of claim 24 in which the *lats* knock-out animal is a mouse.

29. The method of claim 28 in which the *lats* gene contains a lats coding sequence of SEQ ID NO:3.

30. The method of claim 24 in which both alleles of the *lats* gene have been inactivated.

31. The method of claim 24 in which the indicator is fertility.

32. The method of claim 24 in which the indicator is ovulation.

33. The method of claim 24 in which the indicator is linear growth.

34. The method of claim 24 in which the indicator is serum levels of luteinizing hormone, growth hormone or prolactin.

35. The method of claim 24 in which the disease or disorder is LH hypogonadotropic hypogonadism.

36. A method for screening a potential therapeutic compound for activity in treating or preventing a disease or disorder associated with pituitary dysfunction comprising recombinantly expressing the compound in a *lats* knock-out animal; and comparing the level of an indicator of pituitary dysfunction in the *lats* knock-out animal in which the compound has been expressed to the level of the indicator either in the same *lats* knock-out animal prior to expression of the compound or to a *lats* knock-out animal in which the compound has not been expressed or to a standard level of the indicator for such same or a *lats* knock-out animal in which the compound was not so expressed, wherein a change in the indicator toward the level of the indicator in a wild type animal not afflicted with a pituitary dysfunction as compared to the same animal prior to expression of the compound or to the animal in which the compound was not so expressed or to the standard level of the indicator, indicates that the compound is active to treat or prevent a disease or disorder associated with pituitary dysfunction.

37. The method of claim 6, 14 or 24 in which the compound is purified.

38. A method for treating a cancer that has been shown to be refractory to a chemotherapy or radiation therapy in a subject in need of such treatment comprising administering to the subject a therapeutically effective amount of a molecule that promotes lats function.

39. The method of claim 38 in which the subject is a human.

40. The method of claim 38 in which the molecule is a lats protein.

41. The method of claim 38 in which the molecule is a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8.

42. The method of claim 38 in which the molecule is a protein having the amino acid sequence of SEQ ID NO:2.

43. The method of claim 38 in which the molecule is a lats analog or derivative that has activity to promote lats function.

44. The method of claim 38 in which the molecule is a protein encoded by a first nucleic acid that is hybridizable under conditions of low stringency to a second nucleic acid having a nucleotide sequence that is the reverse complement of a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, and SEQ ID NO:7, said protein having activity to inhibit cell overproliferation.

45. The method of claim 38 in which the molecule is a protein consisting of at least 20 contiguous amino acids of a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8, said protein having activity to inhibit cell overproliferation.

46. The method of claim 38 in which the molecule is a protein comprising a domain of a lats protein selected from the group consisting of a lats C-terminal domain 3 (LCD3), lats C-terminal domain 2 (LCD2), lats C-terminal domain 1 (LCD1), kinase domain, lats flanking domain (LFD), lats split domain 1 (LSD1), lats split domain 2 (LSD2), and SH3-binding domain, said protein having activity to inhibit cell overproliferation.

47. The method of claim 40 in which the lats protein is phosphorylated.

48. The method of claim 47 in which the lats protein is phosphorylated on a serine or threonine residue within 20 residues upstream of the amino acid sequence Ala-Pro-Glu in a subdomain eight of a kinase domain of said lats protein.

49. The method of claim 48 in which the lats protein is phosphorylated at a serine residue corresponding to serine 909 of the human lats amino acid sequence, as depicted in Figure 12 (SEQ ID NO:2).

50. The method of claim 43 in which the lats analog or derivative has a threonine or serine residue within 20 residues upstream of the amino acid sequence Ala-Pro-Glu in a

subdomain eight of a kinase domain of said lats analog or derivative substituted with an aspartate or glutamate residue.

51. The method of claim 50 in which the lats analog or derivative has a glutamate residue substituted for a serine residue at the residue corresponding to serine 909 of the human lats amino acid sequence, as depicted in Figure 12 (SEQ ID NO:2).

52. The method of claim 38 in which said molecule is a chimeric protein comprising a fragment of a lats protein, said fragment consisting of at least 20 contiguous amino acids of said lats protein, fused via a covalent bond to an amino acid sequence of a second protein, said second protein not being a lats protein, said chimeric protein having activity to inhibit cell overproliferation.

53. The method of claim 38 in which said cancer has been shown to be refractory to radiation therapy.

54. The method of claim 38 in which said cancer has been shown to be refractory to chemotherapy.

55. The method of claim 54 in which said chemotherapy kills cancer cells during S phase of the cell cycle.

56. The method of claim 54 in which said chemotherapy kills cancer cells during mitosis.

57. The method of claim 38 which further comprises administering one or more chemotherapeutic agents to the subject.

58. The method of claim 57 in which said one or more chemotherapeutic agents are administered concurrently with the administration of said molecule.

59. The method of claim 57 in which said one or more chemotherapeutic agents are administered subsequent to the administration of said molecule.

60. The method of claim 38 in which said molecule is a nucleic acid comprising a nucleotide sequence encoding a lats protein.

61. The method of claim 60 in which said nucleotide sequence is SEQ ID NO:1.

62. The method of claim 60 in which said nucleotide sequence encodes a protein having the amino acid sequence of SEQ ID NO:2.

63. The method of claim 38 in which said molecule is a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid that is the reverse complement of a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, and SEQ ID NO:7.

64. A method for treating a cancer that has been shown to be refractory to a chemotherapy or radiation therapy in a subject in need of such treatment comprising administering to the subject a therapeutically effective amount of a cell that expresses a recombinant nucleic acid that promotes lats function.

65. The method of claim 64 in which said nucleic acid comprises the nucleotide sequence of SEQ ID NO:1.

66. The method of claim 64 in which said nucleic acid comprises a nucleotide sequence encoding a protein having the amino acid sequence of SEQ ID NO:2.

67. A kit comprising in one or more containers a therapeutically effective amount of a molecule selected from the group consisting of a lats protein, a lats derivative, a lats analog, a nucleic acid encoding a lats protein, a nucleic acid encoding a lats derivative, and a nucleic acid encoding a lats analog; and at least one chemotherapeutic agent.

68. A purified complex of a lats protein and a cdc2 protein.

69. The purified complex of claim 68 in which the proteins are human proteins.

70. The purified complex of claim 68 in which the lats protein is phosphorylated.

71. The purified complex of claim 70 in which the lats protein is phosphorylated on a serine or threonine residue within 20 residues upstream of the amino acid sequence Ala-Pro-Glu in a subdomain eight of a kinase domain of said lats protein.

72. The purified complex of claim 71 in which the lats protein is phosphorylated at a serine residue corresponding to serine 909 of the human lats amino acid sequence, as depicted in Figure 12 (SEQ ID NO:2).

73. A purified complex selected from the group consisting of a complex of a derivative of a lats and a cdc2 protein, a complex of a lats protein and a derivative of a cdc2,

and a complex of a derivative of a lats protein and a derivative of a cdc2 protein, in which the derivative of the lats protein is able to form a complex with a wild-type cdc2 protein and the derivative of the cdc2 is able to form a complex with a wild-type lats protein.

74. The purified complex of claim 73 in which the derivative of the lats protein and/or the cdc2 protein is fluorescently labeled.

75. The purified complex of claim 73 in which the lats derivative has a threonine or serine residue within 20 residues upstream of the amino acid sequence Ala-Pro-Glu in a subdomain eight of a kinase domain of said lats derivative substituted with an aspartate or glutamate residue.

76. The purified complex of claim 75 in which the lats derivative has a glutamate residue substituted for a serine residue at the residue corresponding to serine 909 of the human lats amino acid sequence, as depicted in Figure 12 (SEQ ID NO:2).

77. The purified complex of claim 73 in which the lats derivative is a fragment of a lats protein consisting of the amino acid sequence corresponding to amino acids 15-585 of the amino acid sequence of human lats, as depicted in Figure 12 (SEQ ID NO:2).

78. A chimeric protein comprising a fragment of a lats protein consisting of at least 6 amino acids fused via a covalent bond to a fragment of a cdc2 protein consisting of at least 6 amino acids.

79. The chimeric protein of claim 78 in which the fragment of the lats protein is a fragment capable of binding the cdc2 protein and in which the fragment of the cdc2 protein is a fragment capable of binding the lats protein.

80. The chimeric protein of claim 78 in which the fragment of the lats protein has an amino acid sequence corresponding to amino acids 15 to 585 of the amino acid sequence of human lats, as depicted in Figure 12 (SEQ ID NO:2).

81. The chimeric protein of claim 79 in which the fragment of the lats protein and the fragment of the cdc2 protein form a lats-cdc2 complex.

82. An antibody which immunospecifically binds the complex of claim 68 or a fragment or derivative of said antibody containing the binding domain thereof.

83. The antibody of claim 82 which does not immunospecifically bind a lats protein or a cdc2 protein that are not part of a lats-cdc2 complex.

84. An isolated nucleic acid or an isolated combination of nucleic acids comprising a nucleotide sequence encoding a lats protein and a nucleotide sequence encoding a cdc2 protein.

85. The isolated nucleic acid or isolated combination of nucleic acids of claim 84 which are nucleic acid vectors.

86. An isolated nucleic acid that comprises a nucleotide sequence encoding the chimeric protein of claim 78.

87. A cell containing the nucleic acid of claim 84, which nucleic acid is recombinant.

88. A cell containing the nucleic acid of claim 86, which nucleic acid is recombinant.

89. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the complex of claim 68; and a pharmaceutically acceptable carrier.

90. The pharmaceutical composition of claim 89 in which the proteins are human proteins.

91. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the complex of claim 73; and a pharmaceutically acceptable carrier.

92. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the chimeric protein of claim 79; and a pharmaceutically acceptable carrier.

93. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the antibody of claim 83 or a fragment or derivative of said antibody containing the binding domain thereof; and a pharmaceutically acceptable carrier.

94. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the nucleic acids or combination of nucleic acids of claim 84; and a pharmaceutically acceptable carrier.

95. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the isolated nucleic acid of claim 86; and a pharmaceutically acceptable carrier.

96. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the recombinant cell of claim 87; and a pharmaceutically acceptable carrier.

97. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the recombinant cell of claim 88; and a pharmaceutically acceptable carrier.

98. A method of producing a complex of a lats protein and a cdc2 protein comprising growing a recombinant cell containing the nucleic acid of claim 84 such that the encoded lats and cdc2 proteins are expressed and bind to each other, and recovering the expressed complex of the lats protein and the cdc2 protein.

99. A method of diagnosing or screening for the presence of or a predisposition for developing a disease or disorder characterized by an aberrant level of a complex of a lats protein and a cdc2 protein in a subject comprising measuring the level of said complex, RNA encoding the lats and the cdc2 proteins, or functional activity of said complex, in a sample derived from the subject, in which an increase or decrease in the level of said complex, said RNA encoding lats and cdc2, or functional activity of said complex in the sample, relative to the level of said complex, said RNA encoding lats and cdc2, or functional activity of said complex found in an analogous sample from a subject not having the disease or disorder or a predisposition for developing the disease or disorder, indicates the presence of the disease or disorder or a predisposition for developing the disease or disorder.

100. A kit comprising in one or more containers a substance selected from the group consisting of a complex of a lats and a cdc2 protein, an antibody against said complex, nucleic acid probes capable of hybridizing to RNA of lats and RNA of cdc2, or pairs of nucleic acid primers capable of priming amplification of at least a portion of a gene for lats and a gene for cdc2.

101. A method for modulating the activity of cdc2 comprising administering a molecule that promotes, inhibits, or antagonizes lats function.

102. A method for inhibiting the activity of cdc2 comprising administrating a molecule that promotes lats function.

103. A method for increasing the activity of cdc2 comprising administering a molecule that inhibits or antagonizes lats function.

104. A method for treating or preventing a disease or disorder associated with an aberrantly high level of cdc2 in a subject in need of such treatment or prevention comprising administering to the subject a therapeutically effective amount of a molecule that promotes lats function.

105. The method of claim 104 in which said molecule is selected from the group consisting of a lats protein, a lats derivative or analog that promotes lats function, a nucleic acid encoding a lats protein, and nucleic acid encoding a lats derivative or analog that promotes lats function, and a lats agonist.

106. A method for treating or preventing a disease or disorder associated with an aberrantly low level of cdc2 activity in a subject in which such treatment or prevention is desired comprising administering to the subject a therapeutically effective amount of a molecule that inhibits or antagonizes lats function.

107. The method of claim 106 in which said molecule is selected from the group consisting of a lats analog or derivative that inhibits or antagonizes lats function, an anti-lats antibody, and a *lats* antisense nucleic acid.

108. A method for screening a molecule for efficacy in treating or preventing a cancer refractory to chemotherapy or radiation therapy, said method comprising contacting cancer cells that are refractory to treatment with chemotherapeutic agents or radiation with the molecule and comparing the proliferation or survival of the contacted cells with the proliferation or survival of cells not so contacted, wherein a lower level of proliferation or survival of the contacted cells indicates that the molecule is effective to treat or prevent the cancer.

109. The method of claim 108 in which said cells are cultured *in vitro* from a tissue sample of a patient.

110. A method for screening a molecule for activity to modulate cdc2 levels or activity comprising contacting cells with the molecule, and comparing the level of cdc2 protein, mRNA or activity in cells contacted with the molecule to the amount of cdc2 protein, mRNA, or activity in cells not so contacted, wherein an increase or decrease in the amount of cdc2 protein, mRNA, or activity in the contacted cells relative to the amount of cdc2 protein, mRNA, or activity in the cells not so contacted indicates that the molecule has activity to modulate cdc2 levels or activity.

111. A method for screening a molecule for activity to modulate, directly or indirectly, the formation of a complex of lats and cdc2 proteins comprising measuring the levels of said complex formed from lats and cdc2 proteins in the presence of said molecule under conditions conducive to formation of the complex; and comparing the levels of said complex with the levels of said complex that are formed in the absence of said molecule, wherein a lower or higher level of said complex in the presence of said molecule indicates that the molecule modulates formation of said complex.

112. The method of claim 111 in which the molecule inhibits formation of the complex.

113. The method of claim 111 in which the molecule promotes formation of the complex.